# STIC Search Report
## Biotech-Chem Library

**STIC Database Tracking Number: 200613**

| | |
|---|---|
| **TO: Traviss McIntosh**<br>**Location: REM-5C29/5C18**<br>**Art Unit: 1623**<br>**Thursday, September 07, 2006**<br><br>**Case Serial Number: 10/608907** | **From: Alex Waclawiw**<br>**Location: Biotech-Chem Library**<br>**Rem 1A71**<br>**Phone: 272-2534**<br><br>**Alexandra.waclawiw@uspto.gov** |

**Search Notes**

200013

**STIC-Biotech/ChemLib**

**From:** TRAVISS MCINTOSH III [traviss.mcintosh@uspto.gov]
**Sent:** Tuesday, August 29, 2006 8:41 AM
**To:** STIC-Biotech/ChemLib
**Subject:** Database Search Request, Serial Number: 10/608,907

Requester:
TRAVISS MCINTOSH III (P/1623)
Art Unit:
GROUP ART UNIT 1623
Employee Number:
79380
Office Location:
REM 05C29
Phone Number:
(571)272-0657
Mailbox Number:
Rem - 5C29

Case serial number:
10/608,907
Class / Subclass(es):
514/42, 43, 45, 48, 49, 51
Earliest Priority Filing Date:
6/28/2002
Format preferred for results:
E-mail
Search Topic Information:
please search methods of treating viral infections (HCV) with 2'-deoxy, 2'-disubstituted nucleotides/nucleosides, wherein F is in one 2' position and either CH3 or CF3 is in the other 2' position. Base can be purine or pyrimidine. 3' position can be hydroxy, a protected hydroxy group, or a leaving group, and 5' position can be hydroxy, phospho containing, protected hydroxy group, or a leaving group.

Special Instructions and Other Comments:
This is my first search submitted electronically, so if there are better ways, please let me know. I am hoteling, so this will be my standard way to submit searches in the future. I tried to cut and paste or attach the structure to this, but cannot figure out how. If I have to fax the structures in, I will just fax the whole search request in in the future. THanks - Traviss

Point of Contact:
Alexandra Waclawiw
Technical Info. Specialist
CM1 6A02 Tel: 308-4491

**********
Searcher: _____
Searcher Phone: _____
Date Searcher Picked up: 9-7
Date completed: 9-7
Searcher Prep Time: 25
Online Time: 24

**********
Type of Search
NA#_____ AA#:_____
S/L:_____ Oligomer:_____
Encode/Transl:_____
Structure #: 1 Text:____
Inventor:_____ Litigation:___

**********
Vendors and cost where applicable
STN: $ 309
DIALOG:_____
QUESTEL/ORBIT:_____
LEXIS/NEXIS:_____
SEQUENCE SYSTEM:_____
WWW/Internet:_____
Other (Specify):_____

# STIC SEARCH RESULTS FEEDBACK FORM

## Biotech-Chem Library

Questions about the scope or the results of the search? Contact ***the searcher or contact***:

**Mary Hale, Information Branch Supervisor**
**571-272-2507 Remsen 1 A51**

## Voluntary Results Feedback Form

- *I am an examiner in Workgroup:* ☐ *Example: 1610*
- *Relevant prior art **found**, search results used as follows:*
  - ☐ 102 rejection
  - ☐ 103 rejection
  - ☐ Cited as being of interest.
  - ☐ Helped examiner better understand the invention.
  - ☐ Helped examiner better understand the state of the art in their technology.

*Types of relevant prior art found:*

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature
  (journal articles, conference proceedings, new product announcements etc.)

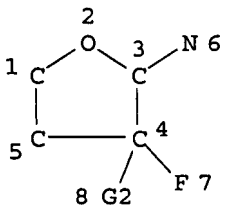
- *Relevant prior art **not found**:*
  - ☐ Results verified the lack of relevant prior art (helped determine patentability).
  - ☐ Results were not useful in determining patentability or understanding the invention.

**Comments:**

**Drop off or send completed forms to STIC/Biotech-Chem Library Remsen Bldg.**

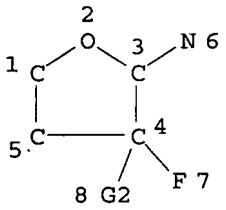
sira
Search and Information Resources Administration

```
=> d his l1-l2;d que stqat l2; d his l3-

     (FILE 'REGISTRY' ENTERED AT 09:28:39 ON 07 SEP 2006)
                DEL HIS Y
                ACT MCINTOSH/A
               ---------
L1               STR
L2            25 SEA FILE=REGISTRY SSS FUL L1


L1               STR
```




```
VAR G2=ME/CF3
NODE ATTRIBUTES:
NSPEC   IS R      AT   6
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS   8

STEREO ATTRIBUTES: NONE
L2            25 SEA FILE=REGISTRY SSS FUL L1

100.0% PROCESSED      43 ITERATIONS                              25 ANSWERS
SEARCH TIME: 00.00.01


     FILE 'CAPLUS' ENTERED AT 09:29:29 ON 07 SEP 2006
L3             7 SEA ABB=ON  PLU=ON  L2
                 D SCAN TI
                 E STORER R/AU
L4           229 SEA ABB=ON  PLU=ON  STORER R?/AU
                 E GOSSELIN G?/AU
L5           317 SEA ABB=ON  PLU=ON  GOSSELIN G?/AU
L6           213 SEA ABB=ON  PLU=ON  SOMMADOSSI J?/AU
L7           694 SEA ABB=ON  PLU=ON  (L4 OR L5 OR L6)
L8             0 SEA ABB=ON  PLU=ON  L7 AND L3
L9        411390 SEA ABB=ON  PLU=ON  NUCLEOTID?/OBI OR NUCLEOSID?/OBI OR
                 FLAVIVIR?/OBI
L10          242 SEA ABB=ON  PLU=ON  L9 AND L7
L11           13 SEA ABB=ON  PLU=ON  L10 AND FLAVIVIR?/OBI
                 D QUE STAT NOS L11
```

```
=> fil reg
FILE 'REGISTRY' ENTERED AT 09:32:47 ON 07 SEP 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:    6 SEP 2006  HIGHEST RN 905963-91-9
DICTIONARY FILE UPDATES:   6 SEP 2006  HIGHEST RN 905963-91-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> d que stat l2
L1              STR
```




```
VAR G2=ME/CF3
NODE ATTRIBUTES:
NSPEC   IS R      AT   6
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS   8

STEREO ATTRIBUTES: NONE
L2            25 SEA FILE=REGISTRY SSS FUL L1

100.0% PROCESSED      43 ITERATIONS                          25 ANSWERS
SEARCH TIME: 00.00.01


=> fil caplus
FILE 'CAPLUS' ENTERED AT 09:32:53 ON 07 SEP 2006
```

FILE COVERS 1907 - 7 Sep 2006 VOL 145 ISS 11
FILE LAST UPDATED: 6 Sep 2006 (20060906/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

```
=> d que nos l3
L1              STR
L2           25 SEA FILE=REGISTRY SSS FUL L1
L3            7 SEA FILE=CAPLUS ABB=ON  PLU=ON  L2


=> => d que stat nos l11
L4          229 SEA FILE=CAPLUS ABB=ON  PLU=ON  STORER R?/AU
L5          317 SEA FILE=CAPLUS ABB=ON  PLU=ON  GOSSELIN G?/AU
L6          213 SEA FILE=CAPLUS ABB=ON  PLU=ON  SOMMADOSSI J?/AU
L7          694 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L4 OR L5 OR L6)
L9       411390 SEA FILE=CAPLUS ABB=ON  PLU=ON  NUCLEOTID?/OBI OR NUCLEOSID?/OB
                I OR FLAVIVIR?/OBI
L10         242 SEA FILE=CAPLUS ABB=ON  PLU=ON  L9 AND L7
L11          13 SEA FILE=CAPLUS ABB=ON  PLU=ON  L10 AND FLAVIVIR?/OBI
```

↳ inventor search

```
=> d .ca hitstr l3 1-7;d bib ab l11 1-13

L3   ANSWER 1 OF 7  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2006:603846  CAPLUS
DOCUMENT NUMBER:          145:76603
TITLE:                    Fluorinated pyrrolo[2,3-d]pyrimidine nucleosides for
                          the treatment of RNA-dependent RNA viral infection
INVENTOR(S):              Maccoss, Malcolm; Olsen, David B.; Leone, Joseph;
                          Durette, Philippe L.
PATENT ASSIGNEE(S):       Merck & Co., Inc., USA
SOURCE:                   PCT Int. Appl., 46 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.        DATE
     ---------------      ----   --------    --------------------   --------
```

WO 2006065335 A2 20060622 WO 2005-US37224 20051017
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-620743P P 20041021
US 2005-651366P P 20050209

OTHER SOURCE(S): MARPAT 145:76603

ED Entered STN: 23 Jun 2006

AB The present invention provides fluorinated pyrrolo[2,3, d]pyrimidine nucleoside compds. which are inhibitors of RNA-dependent RNA viral polymerase. These compds. are inhibitors of RNA-dependent RNA viral replication and are useful for the treatment of RNA-dependent RNA viral infection. They are particularly useful as precursors to inhibitors of hepatitis C virus (HCV) NS5B polymerase, as precursors to inhibitors of HCV replication, and/or for the treatment of hepatitis C infection. The invention also describes pharmaceutical compns. containing such fluorinated pyrrolo[2,3- d]pyrimidine nucleoside alone or in combination with other agents active against RNA-dependent RNA viral infection, in particular HCV infection. Also disclosed are methods of inhibiting RNA-dependent RNA polymerase, inhibiting RNA-dependent RNA viral replication, and/or treating RNA-dependent RNA viral infection with the fluorinated pyrrolo[2,3- d]pyrimidine nucleoside of the present invention.

CC 1-5 (Pharmacology)
Section cross-reference(s): 28

IT **892389-29-6 892389-31-0**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fluorinated pyrrolopyrimidine nucleosides for treatment of RNA-dependent RNA viral infection)

IT 22276-95-5P 443643-17-2P 582313-56-2P 582313-57-3P 729596-49-0P 741686-50-0P 892389-00-3P 892389-02-5P 892389-04-7P 892389-08-1P 892389-12-7P 892389-14-9P 892389-17-2P 892389-19-4P 892389-21-8P 892389-23-0P 892389-25-2P **892389-27-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(fluorinated pyrrolopyrimidine nucleosides for treatment of RNA-dependent RNA viral infection)

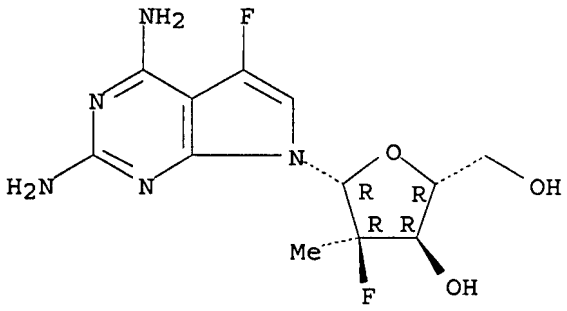
IT 892389-06-9P **892389-10-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(fluorinated pyrrolopyrimidine nucleosides for treatment of RNA-dependent RNA viral infection)

IT **892389-29-6 892389-31-0**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fluorinated pyrrolopyrimidine nucleosides for treatment of RNA-dependent RNA viral infection)

RN 892389-29-6 CAPLUS

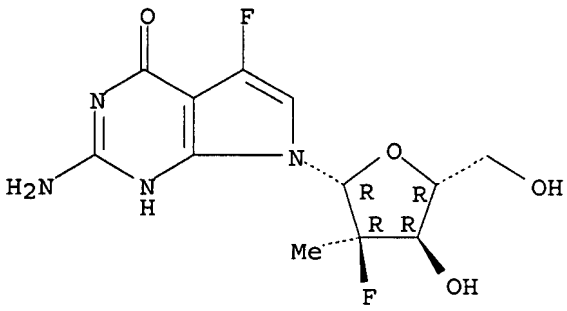
CN 7H-Pyrrolo[2,3-d]pyrimidine-2,4-diamine, 7-[(2R)-2-deoxy-2-fluoro-2-methyl-β-D-erythro-pentofuranosyl]-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



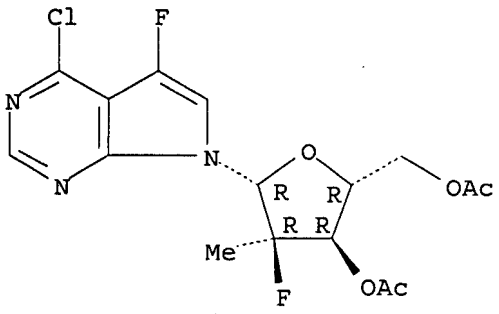
RN 892389-31-0 CAPLUS
CN 4H-Pyrrolo[2,3-d]pyrimidin-4-one, 2-amino-7-[(2R)-2-deoxy-2-fluoro-2-methyl-β-D-erythro-pentofuranosyl]-5-fluoro-1,7-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **892389-27-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(fluorinated pyrrolopyrimidine nucleosides for treatment of RNA-dependent RNA viral infection)
RN 892389-27-4 CAPLUS
CN 7H-Pyrrolo[2,3-d]pyrimidine, 4-chloro-7-[(2R)-3,5-di-O-acetyl-2-deoxy-2-fluoro-2-methyl-β-D-erythro-pentofuranosyl]-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



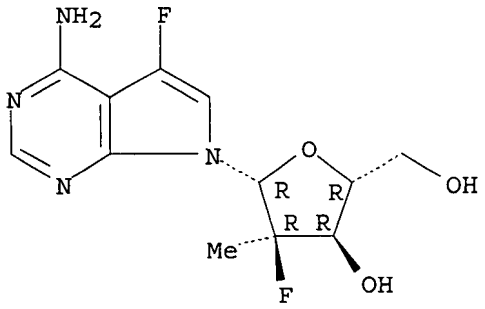
IT **892389-10-5P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(fluorinated pyrrolopyrimidine nucleosides for treatment of RNA-dependent RNA viral infection)

RN 892389-10-5 CAPLUS

CN 7H-Pyrrolo[2,3-d]pyrimidin-4-amine, 7-[(2R)-2-deoxy-2-fluoro-2-methyl-β-D-erythro-pentofuranosyl]-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.




L3 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:478128 CAPLUS

DOCUMENT NUMBER: 145:202057

TITLE: Inhibition of hepatitis C replicon RNA synthesis by β-D-2'-deoxy-2'-fluoro-2'-C-methylcytidine: a specific inhibitor of hepatitis C virus replication

AUTHOR(S): Stuyver, Lieven J.; McBrayer, Tamara R.; Tharnish, Phillip M.; Clark, Jeremy; Hollecker, Laurent; Lostia, Stefania; Nachman, Tammy; Grier, Jason; Bennett, Matthew A.; Xie, Meng-Yu; Schinazi, Raymond F.; Morrey, John D.; Julander, Justin L.; Furman, Phillip A.; Otto, Michael J.

CORPORATE SOURCE: Pharmasset Inc, Princeton, NJ, USA

SOURCE: Antiviral Chemistry & Chemotherapy (2006), 17(2), 79-87
CODEN: ACCHEH; ISSN: 0956-3202

PUBLISHER: International Medical Press, Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 22 May 2006

AB β-D-2'-Deoxy-2'-fluoro-2'-C-methylcytidine (PSI-6130) is a cytidine analog with potent and selective anti-hepatitis C virus (HCV) activity in the subgenomic HCV replicon assay, 90% effective concentration (EC90) = 4.6 ± 2.0 μM. The spectrum of activity and cytotoxicity profile of PSI-6130 was evaluated against a diverse panel of viruses and cell types, and against two addnl. HCV-1b replicons. The S282T mutation, which confers resistance to 2'-C-Me adenosine and other 2'-methylated nucleosides, showed only a 6.5-fold increase in EC90. When assayed for activity against bovine diarrhoea virus (BVDV), which is typically used as a surrogate assay to identify compds. active against HCV, PSI-6130 showed no anti-BVDV activity. Weak antiviral activity was noted against other flaviviruses, including West Nile virus, Dengue type 2, and yellow fever virus. These results indicate that PSI-6130 is a specific inhibitor of HCV. PSI-6130 showed little or no cytotoxicity against various cell types, including human peripheral blood mononuclear and human bone marrow progenitor cells. No mitochondrial toxicity was observed with PSI-6130. The reduced activity against the RdRp S282T mutant suggests that PSI-6130 is

an inhibitor of replicon RNA synthesis. Finally, the no-effect dose for mice treated i.p. with PSI-6130 for six consecutive days was ≥100 mg/kg per day.

CC 1-5 (Pharmacology)

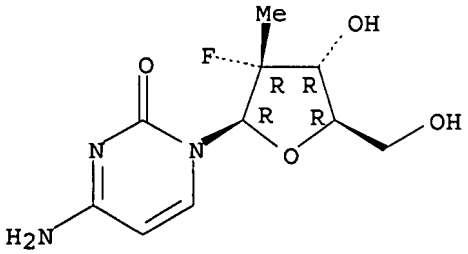
IT **817204-33-4**, PSI 6130
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PSI-6130 inhibition of hepatitis C replicon RNA synthesis)

IT **817204-33-4**, PSI 6130
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PSI-6130 inhibition of hepatitis C replicon RNA synthesis)

RN 817204-33-4 CAPLUS

CN Cytidine, 2'-deoxy-2'-fluoro-2'-methyl-, (2'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).




REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:269477 CAPLUS

DOCUMENT NUMBER: 144:312289

TITLE: Preparation of alkyl-substituted 2-deoxy-2-fluoro-D-ribofuranosyl pyrimidine and purine nucleoside analogs via condensation of the lactone to nucleosides as potential antiviral agents

INVENTOR(S): Chun, Byoung-Kwon; Wang, Peiyuan

PATENT ASSIGNEE(S): Pharmasset, Inc., USA

SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006031725 | A2 | 20060323 | WO 2005-US32406 | 20050913 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,

IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

US 2006122146 A1 20060608 US 2005-225425 20050913
PRIORITY APPLN. INFO.: US 2004-609783P P 20040914
US 2004-610035P P 20040915
US 2005-666230P P 20050329

OTHER SOURCE(S): MARPAT 144:312289
ED Entered STN: 23 Mar 2006
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A process for preparing of 2-deoxy-2-fluoro-2-methyl-D-ribonolactones, I, wherein R1 and R2 can independently be H, CH3, acetyl, benzoyl, pivaloyl, 4-nitrobenzoyl, 3-nitrobenzoyl, 2-nitrobenzoyl, 4-chlorobenzoyl, 3-chlorobenzoyl, 2-chlorobenzoyl, 4-methylbenzoyl, 3-methylbenzoyl, 2-methylbenzoyl, 4-phenylbenzoyl, benzyl, 4-methoxybenzyl, trityl, trialkylsilyl, t-butyl-dialkylsilyl, t-butyldiphenylsilyl, TIPDS, THP, MOM, or MEM are prepared and used in the condensation to 2-deoxy-2-fluoro-D-ribofuranosyl pyrimidine and purine nucleoside analogs. Thus, 2-deoxy-2-fluoro-D-ribofuranosyl pyrimidine and purine nucleoside analogs II and III, wherein X is a halogen; Y is N or CH; Z is a halogen, hydroxyl, ether, thiol, thioether, (un)substituted amine or alkyl; R1' is alkyl, vinyl, ethynyl; R2' and R3' can be same or different H, alkyl, arylalkyl, acyl, cyclic acetal such as 2',3'-O-isopropylidene or 2',3-O-benzylidene, or 2',3'-cyclic carbonate; R4, R5, and R6 are independently H, halogen, hydroxyl, ether, thiol, thioether, N3, (un)substituted amine, (un)substituted amido, alkyl, halogenated alkyl, alkenyl, halogenated alkenyl, alkynyl, halogenated alkynyl, hydroxy alkyl, alkoxy are prepared and are potential anti-HCV agents. Specifically, IV was prepared in 88 % yield via condensation, alkylation and stereoselective fluorination reactions and can exhibit potential use as an anti-HCV agent.

CC 33-9 (Carbohydrates)
Section cross-reference(s): 1, 63

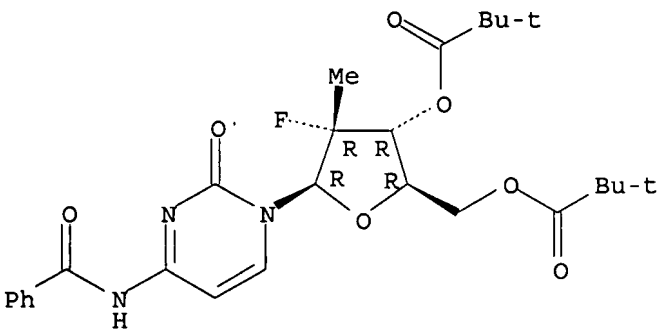
IT 874638-80-9P 879551-05-0P **879551-07-2P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of alkyl-substituted 2-deoxy-2-fluoro-D-ribofuranosyl pyrimidine and purine nucleoside analogs via condensation of the lactone to nucleosides)

IT **879551-07-2P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of alkyl-substituted 2-deoxy-2-fluoro-D-ribofuranosyl pyrimidine and purine nucleoside analogs via condensation of the lactone to nucleosides)

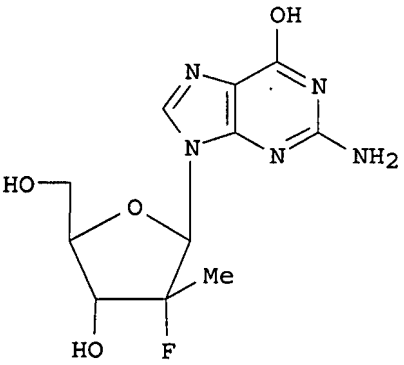
RN 879551-07-2 CAPLUS

CN Cytidine, N-benzoyl-2'-deoxy-2'-fluoro-2'-methyl-, 3',5'-bis(2,2-dimethylpropanoate), (2'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:128527 CAPLUS
DOCUMENT NUMBER: 144:370341
TITLE: Synthesis and antiviral activity of 2'-deoxy-2'-fluoro-2'-C-methyl purine nucleosides as inhibitors of hepatitis C virus RNA replication
AUTHOR(S): Clark, Jeremy L.; Mason, J. Christian; Hollecker, Laurent; Stuyver, Lieven J.; Tharnish, Phillip M.; McBrayer, Tamara R.; Otto, Michael J.; Furman, Phillip A.; Schinazi, Raymond F.; Watanabe, Kyoichi A.
CORPORATE SOURCE: Pharmasset, Inc., Tucker, GA, 30084, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(6), 1712-1715
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 144:370341
ED Entered STN: 12 Feb 2006
GI



I

AB A series of purine nucleosides, e.g. I, containing the 2'-deoxy-2'-fluoro-2'-C-methylribofuranosyl moiety were synthesized and evaluated as potential inhibitors of the hepatitis C virus in vitro. Of the nucleosides that were synthesized, only those possessing a 2-amino group on the purine base reduced the levels of HCV RNA in a sub-genomic replicon assay.
CC 33-9 (Carbohydrates)

Section cross-reference(s): 1, 3, 6

IT **881881-89-6P**
RL: BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and antiviral activity of deoxyfluoromethyl purine nucleosides as inhibitors of hepatitis C virus RNA replication)

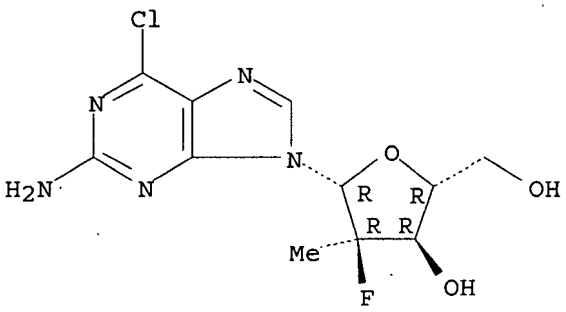
IT 15397-12-3P 374750-30-8P **817204-42-5P 817204-45-8P 818374-78-6P**
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and antiviral activity of deoxyfluoromethyl purine nucleosides as inhibitors of hepatitis C virus RNA replication)

IT **817204-41-4P 881881-83-0P** 881881-84-1P 881881-85-2P **881881-88-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and antiviral activity of deoxyfluoromethyl purine nucleosides as inhibitors of hepatitis C virus RNA replication)

IT **881881-89-6P**
RL: BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and antiviral activity of deoxyfluoromethyl purine nucleosides as inhibitors of hepatitis C virus RNA replication)

RN 881881-89-6 CAPLUS
CN 9H-Purin-2-amine, 6-chloro-9-[(2R)-2-deoxy-2-fluoro-2-methyl-β-D-erythro-pentofuranosyl]- (9CI) (CA INDEX NAME)

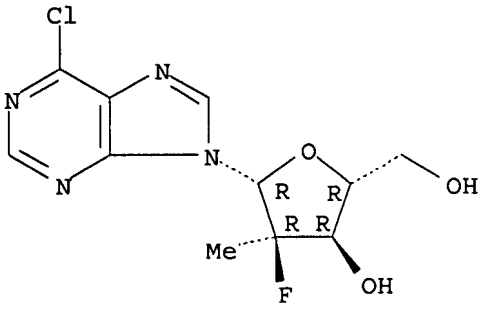
Absolute stereochemistry.




IT **817204-42-5P 817204-45-8P 818374-78-6P**
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and antiviral activity of deoxyfluoromethyl purine nucleosides as inhibitors of hepatitis C virus RNA replication)

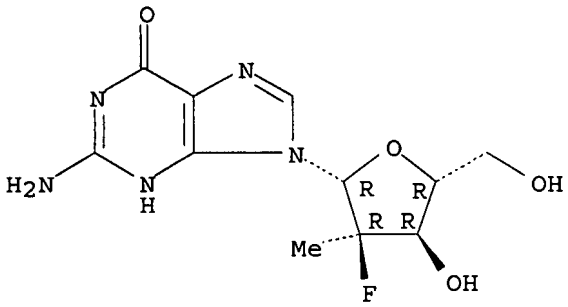
RN 817204-42-5 CAPLUS
CN 9H-Purine, 6-chloro-9-[(2R)-2-deoxy-2-fluoro-2-methyl-β-D-erythro-pentofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



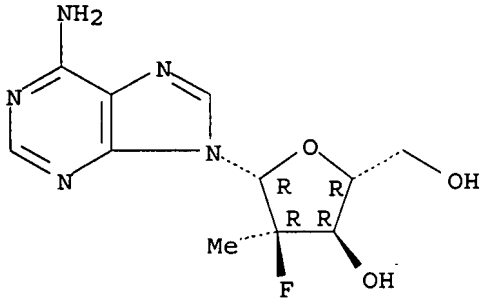
RN 817204-45-8 CAPLUS
CN Guanosine, 2'-deoxy-2'-fluoro-2'-methyl-, (2'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



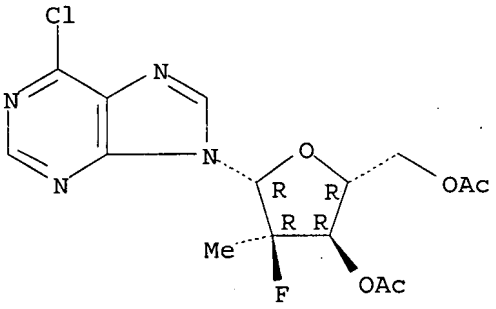
RN 818374-78-6 CAPLUS
CN Adenosine, 2'-deoxy-2'-fluoro-2'-methyl-, (2'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



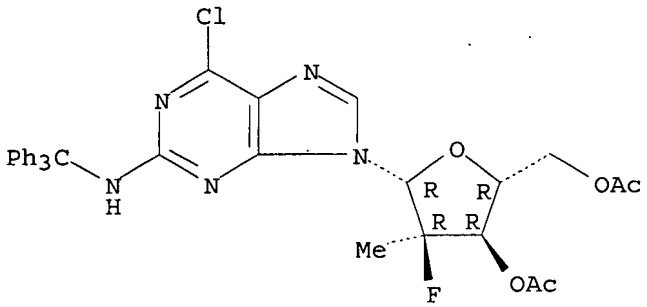
IT **817204-41-4P 881881-83-0P 881881-88-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and antiviral activity of deoxyfluoromethyl purine nucleosides as inhibitors of hepatitis C virus RNA replication)
RN 817204-41-4 CAPLUS
CN 9H-Purine, 6-chloro-9-[(2R)-3,5-di-O-acetyl-2-deoxy-2-fluoro-2-methyl-β-D-erythro-pentofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



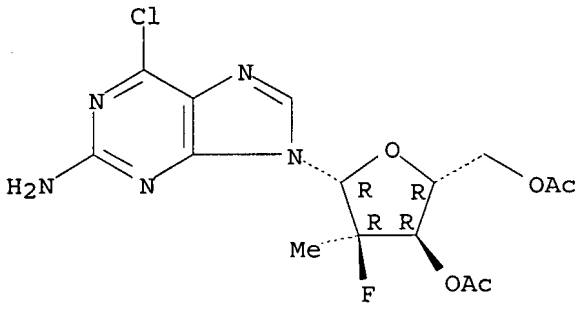
RN 881881-83-0 CAPLUS
CN 9H-Purin-2-amine, 6-chloro-9-[(2R)-3,5-di-O-acetyl-2-deoxy-2-fluoro-2-methyl-β-D-erythro-pentofuranosyl]-N-(triphenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 881881-88-5 CAPLUS
CN 9H-Purin-2-amine, 6-chloro-9-[(2R)-3,5-di-O-acetyl-2-deoxy-2-fluoro-2-methyl-β-D-erythro-pentofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:103884 CAPLUS
DOCUMENT NUMBER: 144:171198
TITLE: Preparation of alkyl-substituted 2-deoxy-2-fluoro-D-

ribofuranosyl pyrimidine and purine nucleoside analogs via condensation of the lactone to nucleosides as potential antiviral agents

INVENTOR(S): Wang, Peiyuan; Stec, Wojciech; Clark, Jeremy; Chun, Byoung-Kwon; Shi, Junxing; Du, Jinfa

PATENT ASSIGNEE(S): Pharmasset, Inc., USA

SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006012440 | A2 | 20060202 | WO 2005-US25916 | 20050721 |
| WO 2006012440 | A3 | 20060727 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-589866P P 20040721
US 2004-608320P P 20040909

OTHER SOURCE(S): MARPAT 144:171198

ED Entered STN: 03 Feb 2006

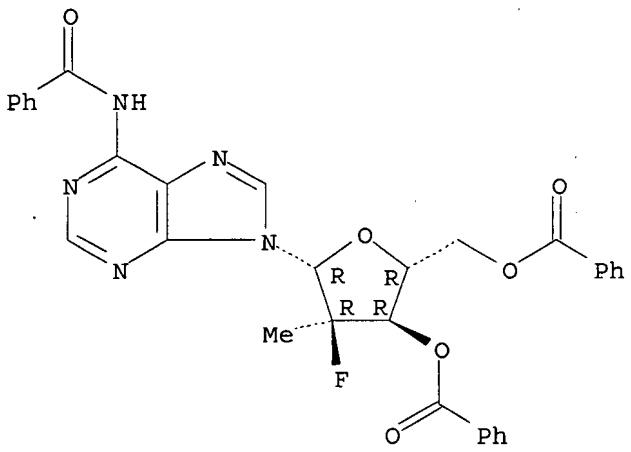
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A process for preparing of 2-deoxy-2-fluoro-2-methyl-D-ribonolactones, I, wherein R1 and R2 can independently be H, CH3, acetyl, benzoyl, pivaloyl, 4-nitrobenzoyl, 3-nitrobenzoyl, 2-nitrobenzoyl, 4-chlorobenzoyl, 3-chlorobenzoyl, 2-chlorobenzoyl, 4-methylbenzoyl, 3-methylbenzoyl, 2-methylbenzoyl, 4-phenylbenzoyl, benzyl, 4-methoxybenzyl, trityl, trialkylsilyl, t-butyl-dialkylsilyl, t-butyldiphenylsilyl, TIPDS, THP, MOM, or MEM are prepared and used in the condensation to 2-deoxy-2-fluoro-D-ribofuranosyl pyrimidine and purine nucleoside analogs. Thus, 2-deoxy-2-fluoro-D-ribofuranosyl pyrimidine and purine nucleoside analogs II and III, wherein X is a halogen; Y is N or CH; Z is a halogen, hydroxyl, ether, thiol, thioether, (un)substituted amine or alkyl; R1' is alkyl, vinyl, ethynyl; R2' and R3' can be same or different H, alkyl, arylalkyl, acyl, cyclic acetal such as 2',3'-O-isopropylidene or 2',3-O-benzylidene, or 2',3'-cyclic carbonate; R4, R5, and R6 are independently H, halogen, hydroxyl, ether, thiol, thioether, N3, (un)substituted amine, (un)substituted amido, alkyl, halogenated alkyl, alkenyl, halogenated alkenyl, alkynyl, halogenated alkynyl, hydroxy alkyl, alkoxy are prepared and are potential anti-HCV agents. Specifically, IV was prepared (no yield, claimed) via condensation, alkylation and stereoselective fluorination reactions and can exhibit potential use as an

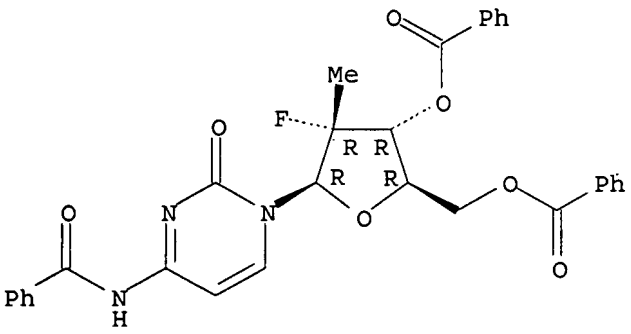
anti-HCV agent.
CC 33-9 (Carbohydrates)
Section cross-reference(s): 1, 63
IT 53008-90-5P 81997-76-4P 93635-76-8P 135120-06-8P 874638-79-6P
874638-80-9P 874638-81-0P 874638-84-3P 874638-85-4P 874638-86-5P
874638-87-6P 874638-89-8P 874638-90-1P 874638-91-2P 874638-93-4P
874638-96-7P **874638-97-8P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of alkyl-substituted 2-deoxy-2-fluoro-D-ribofuranosyl pyrimidine and purine nucleoside analogs via condensation of the lactone to nucleosides)
IT 729596-46-7P **817204-32-3P 817204-33-4P**
**874638-82-1P** 874638-83-2P 874638-88-7P 874638-92-3P
**874638-94-5P 874638-95-6P 874638-98-9P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of alkyl-substituted 2-deoxy-2-fluoro-D-ribofuranosyl pyrimidine and purine nucleoside analogs via condensation of the lactone to nucleosides)
IT **874638-97-8P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of alkyl-substituted 2-deoxy-2-fluoro-D-ribofuranosyl pyrimidine and purine nucleoside analogs via condensation of the lactone to nucleosides)
RN 874638-97-8 CAPLUS
CN Adenosine, N-benzoyl-2'-deoxy-2'-fluoro-2'-methyl-, 3',5'-dibenzoate, (2'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



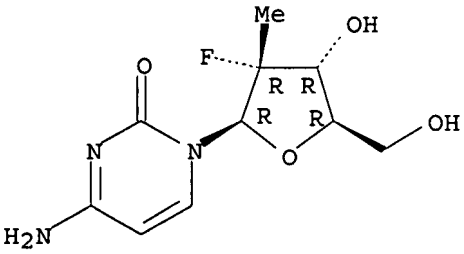

IT **817204-32-3P 817204-33-4P 874638-82-1P**
**874638-94-5P 874638-95-6P 874638-98-9P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of alkyl-substituted 2-deoxy-2-fluoro-D-ribofuranosyl pyrimidine and purine nucleoside analogs via condensation of the lactone to nucleosides)
RN 817204-32-3 CAPLUS
CN Cytidine, N-benzoyl-2'-deoxy-2'-fluoro-2'-methyl-, 3',5'-dibenzoate, (2'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



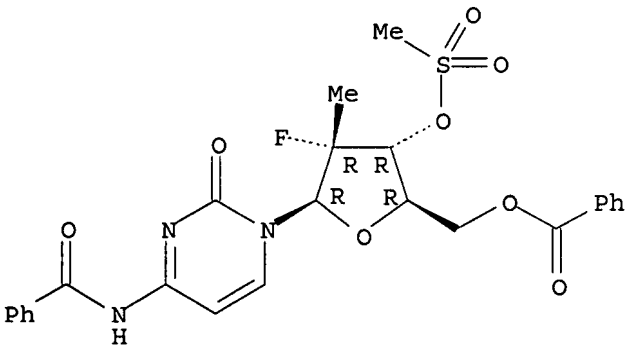
RN 817204-33-4 CAPLUS
CN Cytidine, 2'-deoxy-2'-fluoro-2'-methyl-, (2'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



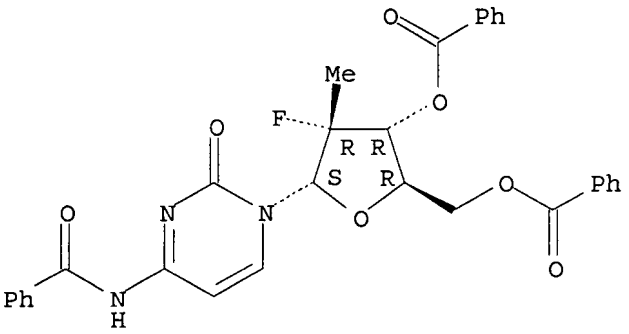
RN 874638-82-1 CAPLUS
CN Benzamide, N-[1-[(2R)-5-O-benzoyl-2-deoxy-2-fluoro-2-methyl-3-O-(methylsulfonyl)-β-D-erythro-pentofuranosyl]-1,2-dihydro-2-oxo-4-pyrimidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



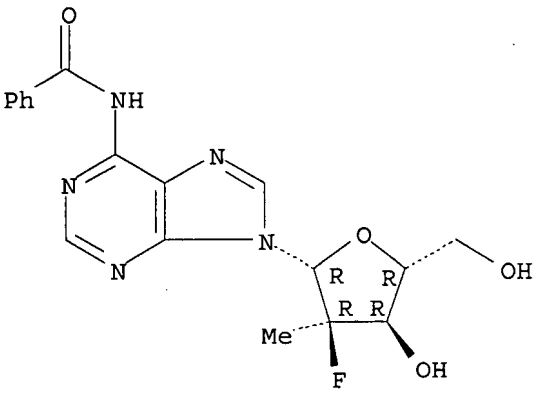
RN 874638-94-5 CAPLUS
CN Benzamide, N-[1-[(2R)-3,5-di-O-benzoyl-2-deoxy-2-fluoro-2-methyl-α-D-erythro-pentofuranosyl]-1,2-dihydro-2-oxo-4-pyrimidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



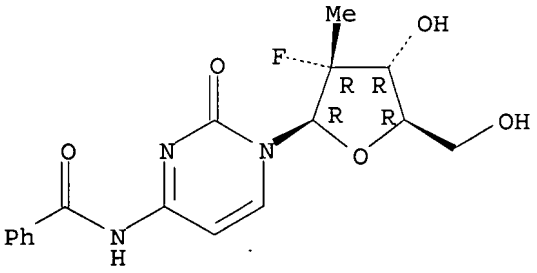
RN 874638-95-6 CAPLUS
CN Adenosine, N-benzoyl-2'-deoxy-2'-fluoro-2'-methyl-, (2'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 874638-98-9 CAPLUS
CN Cytidine, N-benzoyl-2'-deoxy-2'-fluoro-2'-methyl-, (2'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:648160 CAPLUS
DOCUMENT NUMBER: 143:248607
TITLE: Design, Synthesis, and Antiviral Activity of

2'-Deoxy-2'-fluoro-2'-C-methyl-cytidine, a Potent Inhibitor of Hepatitis C Virus Replication

AUTHOR(S): Clark, Jeremy L.; Hollecker, Laurent; Mason, J. Christian; Stuyver, Lieven J.; Tharnish, Phillip M.; Lostia, Stefania; McBrayer, Tamara R.; Schinazi, Raymond F.; Watanabe, Kyoichi A.; Otto, Michael J.; Furman, Phillip A.; Stec, Wojciech J.; Patterson, Steven E.; Pankiewicz, Krzysztof W.

CORPORATE SOURCE: Pharmasset, Inc., Princeton, NJ, 08540, USA

SOURCE: Journal of Medicinal Chemistry (2005), 48(17), 5504-5508
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 26 Jul 2005

AB The pyrimidine nucleoside- β-D-2'-deoxy-2'-fluoro-2'-C-methylcytidine (I) was designed as a hepatitis C virus RNA-dependent RNA polymerase (HCV RdRp) inhibitor. The title compound was obtained by a DAST fluorination of N4-benzoyl-1-(2-methyl-3,5-di-O-benzoyl-β-D-arabinofuranosyl)cytosine to provide N4-benzoyl-1-(2-fluoro-2-methyl-3,5-di-O-benzoyl-β-D-ribofuranosyl)cytosine. The protected 2'-C-methylcytidine was obtained as a byproduct from the DAST fluorination and allowed for the preparation of two biol. active compds. from a common precursor. Compound I and 2'-C-methylcytidine were assayed in a sub-genomic HCV replicon assay system and found to be potent and selective inhibitors of HCV replication. Compd.I shows increased inhibitory activity in the HCV replicon assay compared to 2'-C-methylcytidine and low cellular toxicity.

CC 33-9 (Carbohydrates)
Section cross-reference(s): 1, 7

IT **817204-33-4P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(design, synthesis via fluorination, and antiviral activity of 2'-deoxy-2'-fluoro-2'-C-methyl-cytidine, a potent inhibitor of Hepatitis C virus replication)

IT **863329-66-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(design, synthesis via fluorination, and antiviral activity of 2'-deoxy-2'-fluoro-2'-C-methyl-cytidine, a potent inhibitor of Hepatitis C virus replication)

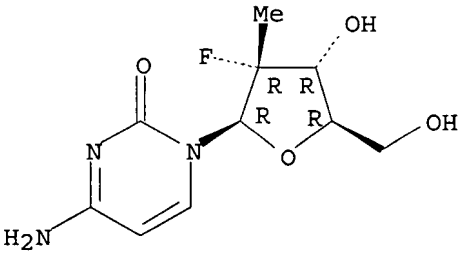
IT **817204-32-3P** 817204-34-5P 817204-35-6P 863329-62-8P 863329-63-9P 863329-64-0P **863329-65-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(design, synthesis via fluorination, and antiviral activity of 2'-deoxy-2'-fluoro-2'-C-methyl-cytidine, a potent inhibitor of Hepatitis C virus replication)

IT 119804-96-5P **817204-38-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(design, synthesis via fluorination, and antiviral activity of 2'-deoxy-2'-fluoro-2'-C-methyl-cytidine, a potent inhibitor of Hepatitis C virus replication)

IT **817204-33-4P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(design, synthesis via fluorination, and antiviral activity of

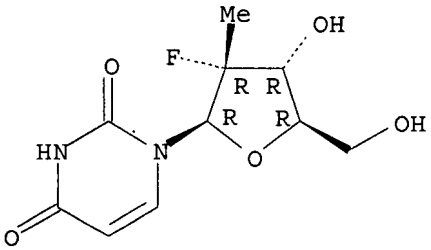
2'-deoxy-2'-fluoro-2'-C-methyl-cytidine, a potent inhibitor of Hepatitis C virus replication)
RN 817204-33-4 CAPLUS
CN Cytidine, 2'-deoxy-2'-fluoro-2'-methyl-, (2'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



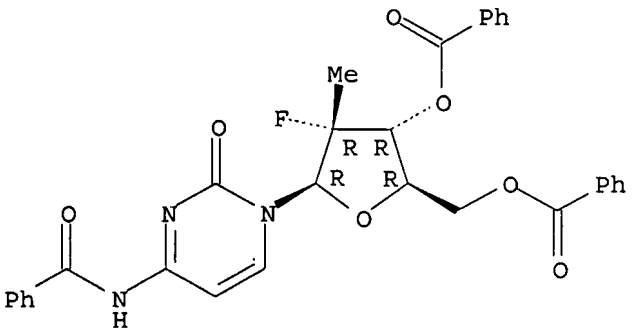

IT **863329-66-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(design, synthesis via fluorination, and antiviral activity of 2'-deoxy-2'-fluoro-2'-C-methyl-cytidine, a potent inhibitor of Hepatitis C virus replication)
RN 863329-66-2 CAPLUS
CN Uridine, 2'-deoxy-2'-fluoro-2'-methyl-, (2'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



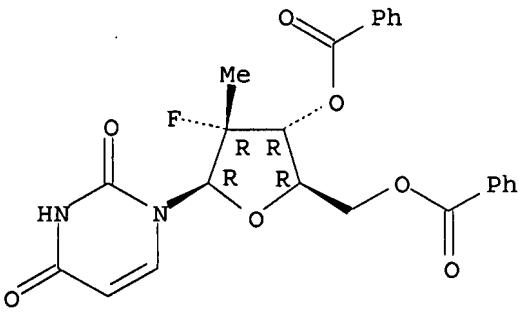

IT **817204-32-3P 863329-65-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(design, synthesis via fluorination, and antiviral activity of 2'-deoxy-2'-fluoro-2'-C-methyl-cytidine, a potent inhibitor of Hepatitis C virus replication)
RN 817204-32-3 CAPLUS
CN Cytidine, N-benzoyl-2'-deoxy-2'-fluoro-2'-methyl-, 3',5'-dibenzoate, (2'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



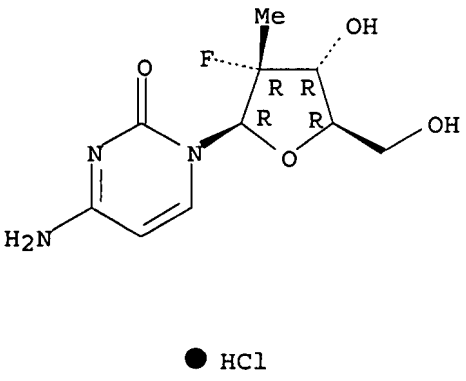
RN 863329-65-1 CAPLUS
CN Uridine, 2'-deoxy-2'-fluoro-2'-methyl-, 3',5'-dibenzoate, (2'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT **817204-38-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(design, synthesis via fluorination, and antiviral activity of 2'-deoxy-2'-fluoro-2'-C-methyl-cytidine, a potent inhibitor of Hepatitis C virus replication)
RN 817204-38-9 CAPLUS
CN Cytidine, 2'-deoxy-2'-fluoro-2'-methyl-, monohydrochloride, (2'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



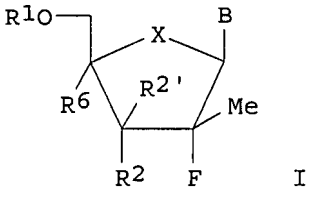
● HCl

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:34765 CAPLUS
DOCUMENT NUMBER: 142:94074
TITLE: Preparation of modified fluorinated (2'R)-2'-deoxy-2'-fluoro-2'-C-methyl nucleoside analogs as antiviral agents
INVENTOR(S): Clark, Jeremy
PATENT ASSIGNEE(S): Pharmasset, Ltd., Barbados
SOURCE: PCT Int. Appl., 228 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| WO 2005003147 | A2 | 20050113 | WO 2004-US12472 | | 20040421 |
| WO 2005003147 | A3 | 20050303 | | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | | |
| AU 2004253860 | A1 | 20050113 | AU 2004-253860 | | 20040421 |
| CA 2527657 | AA | 20050113 | CA 2004-2527657 | | 20040421 |
| US 2005009737 | A1 | 20050113 | US 2004-828753 | | 20040421 |
| EP 1633766 | A2 | 20060315 | EP 2004-775900 | | 20040421 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR | | | | | |
| BR 2004010846 | A | 20060627 | BR 2004-10846 | | 20040421 |
| CN 1816558 | A | 20060809 | CN 2004-80019148 | | 20040421 |
| NO 2005006221 | A | 20051228 | NO 2005-6221 | | 20051228 |
| PRIORITY APPLN. INFO.: | | | US 2003-474368P | P | 20030530 |
| | | | WO 2004-US12472 | W | 20040421 |

OTHER SOURCE(S): MARPAT 142:94074
ED Entered STN: 14 Jan 2005
GI




I

AB The disclosed invention provides nucleoside analogs I, wherein B is purine

and pyrimidine nucleobase; X is O, S, CH2, Se, NH, N-alkyl, CHW, C(W)2; W is F, Cl, Br, iodo; R1 is H, phosphate, H-phosphonate, acyl, Ph, alkyl, carboxyalkylamino, sulfonate ester, peptide, amino acid, sugar reside; R2 and R2' are independently H, alkyl, alkenyl, alkynyl, vunyl, N3, CN, halogen, NO2, ester, alkoxy, thioalkyl, sulfoxide, sulfonyl; R6 is alkyl, CN, Me, OMe, OEt, CH2OH, CH2F, N3, CHCN, CH2N3, CH2NH2, CH2NHMe, CH2NMe2, alkylne; and methods of treating a Flaviviridae infection, including hepatitis C virus, West Nile Virus, yellow fever virus, and a rhinovirus infection in a host, including animals, and especially human, using a (2'R)-2'-deoxy-2'-fluoro-2'-C-Me nucleosides, or a pharmaceutically acceptable salt or prodrug thereof. Thus, (2'R)-2'-deoxy-2'-fluoro-2'-C-methylcytidine was prepared and tested as antiviral agent. The effects the nucleoside analogs tested on human bone marrow cells are reported. (2'R)-2'-deoxy-2'-fluoro-2'-C-methylcytidine shows activity against Rhinovirus, West Nile virus, Yellow Fever virus, and Dengue virus. Cytotoxicity and effect of nucleoside analogs on human bone marrow cells are reported.

IC ICM C07H019-00

CC 33-9 (Carbohydrates)
Section cross-reference(s): 1, 63

IT **817204-33-4P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of modified fluorinated (2'R)-2'-deoxy-2'-fluoro-2'-C-Me nucleoside analogs as antiviral agents)

IT **817204-38-9P 817204-42-5P 817204-43-6P**
**817204-45-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of modified fluorinated (2'R)-2'-deoxy-2'-fluoro-2'-C-Me nucleoside analogs as antiviral agents)

IT 15397-12-3 20724-73-6 374750-27-3 374750-28-4 **817204-44-7**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of modified fluorinated (2'R)-2'-deoxy-2'-fluoro-2'-C-Me nucleoside analogs as antiviral agents)

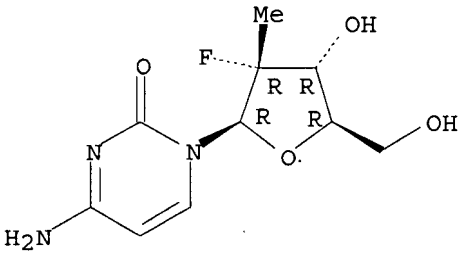
IT 13089-48-0P 69304-43-4P 103285-18-3P 119411-03-9P 129932-37-2P
817204-29-8P 817204-30-1P 817204-31-2P **817204-32-3P**
817204-34-5P 817204-35-6P 817204-36-7P **817204-37-8P**
817204-39-0P 817204-40-3P **817204-41-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of modified fluorinated (2'R)-2'-deoxy-2'-fluoro-2'-C-Me nucleoside analogs as antiviral agents)

IT **817204-33-4P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of modified fluorinated (2'R)-2'-deoxy-2'-fluoro-2'-C-Me nucleoside analogs as antiviral agents)

RN 817204-33-4 CAPLUS

CN Cytidine, 2'-deoxy-2'-fluoro-2'-methyl-, (2'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

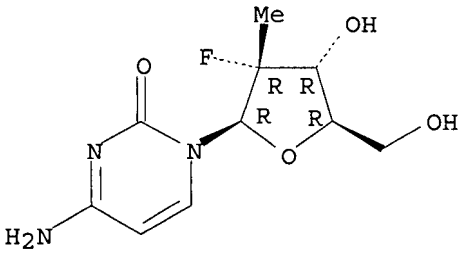


IT **817204-38-9P 817204-42-5P 817204-43-6P**
**817204-45-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of modified fluorinated (2'R)-2'-deoxy-2'-fluoro-2'-C-Me nucleoside analogs as antiviral agents)

RN 817204-38-9 CAPLUS

CN Cytidine, 2'-deoxy-2'-fluoro-2'-methyl-, monohydrochloride, (2'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

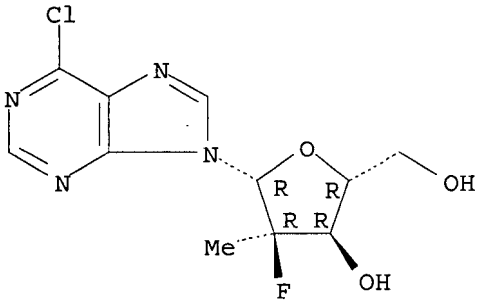


● HCl

RN 817204-42-5 CAPLUS

CN 9H-Purine, 6-chloro-9-[(2R)-2-deoxy-2-fluoro-2-methyl-β-D-erythro-pentofuranosyl]- (9CI) (CA INDEX NAME)

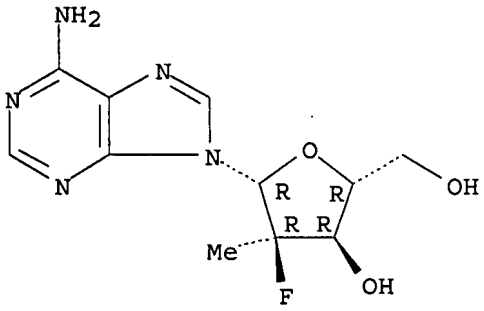
Absolute stereochemistry.



RN 817204-43-6 CAPLUS

CN Adenosine, 2'-deoxy-2'-fluoro-2'-methyl-, monohydrochloride, (2'R)- (9CI) (CA INDEX NAME)

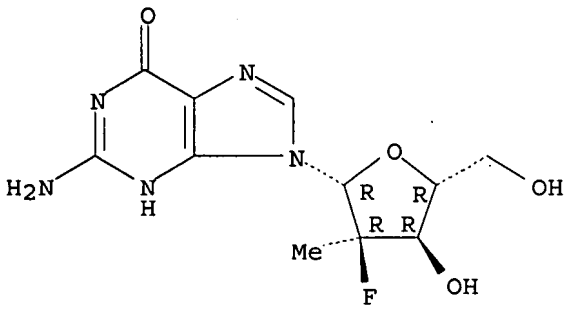
Absolute stereochemistry.



● HCl

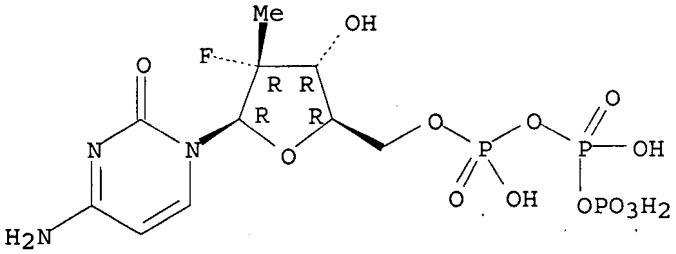
RN 817204-45-8 CAPLUS
CN Guanosine, 2'-deoxy-2'-fluoro-2'-methyl-, (2'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **817204-44-7**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of modified fluorinated (2'R)-2'-deoxy-2'-fluoro-2'-C-Me nucleoside analogs as antiviral agents)
RN 817204-44-7 CAPLUS
CN Cytidine 5'-(tetrahydrogen triphosphate), 2'-deoxy-2'-fluoro-2'-methyl-, (2'R)- (9CI) (CA INDEX NAME)

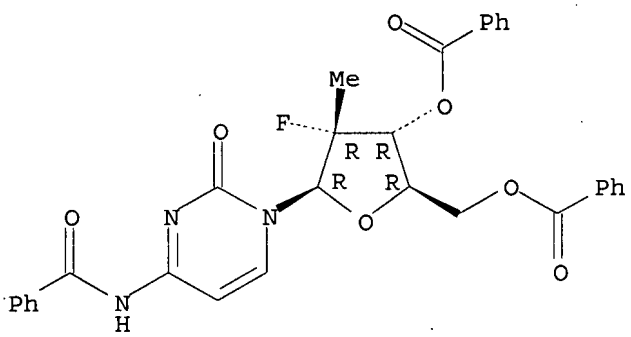
Absolute stereochemistry.



IT **817204-32-3P 817204-37-8P 817204-41-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of modified fluorinated (2'R)-2'-deoxy-2'-fluoro-2'-C-Me nucleoside analogs as antiviral agents)

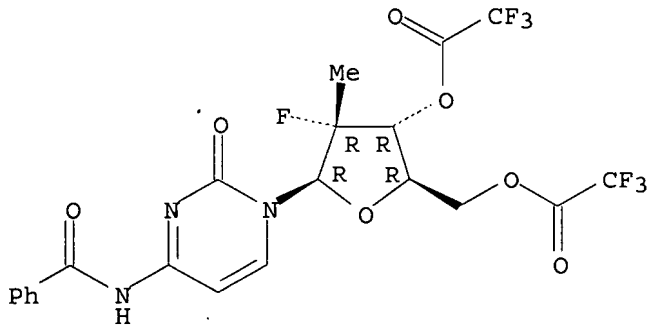
RN 817204-32-3 CAPLUS
CN Cytidine, N-benzoyl-2'-deoxy-2'-fluoro-2'-methyl-, 3',5'-dibenzoate, (2'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



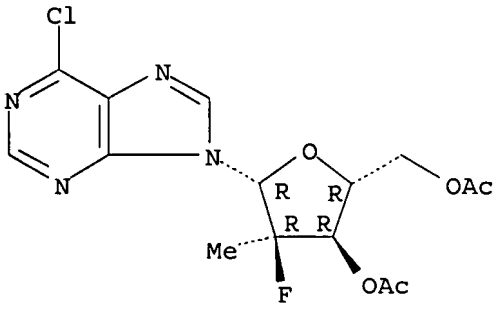
RN 817204-37-8 CAPLUS
CN Cytidine, N-benzoyl-2'-deoxy-2'-fluoro-2'-methyl-, 3',5'-bis(trifluoroacetate), (2'R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 817204-41-4 CAPLUS
CN 9H-Purine, 6-chloro-9-[(2R)-3,5-di-O-acetyl-2-deoxy-2-fluoro-2-methyl-β-D-erythro-pentofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.




=> d bib ab l11 1-13

L11 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2006:316806 CAPLUS
DN 144:331664
TI Preparation of **nucleoside** analogs as antiviral agents for treating **flaviviruses**, pestiviruses and hepacivirus
IN **Sommadossi, Jean-Pierre**; **Gosselin, Gilles**; **Storer, Richard**; Egan, James
PA Idenix (Cayman) Limited, Cayman I.; Centre National de la Recherche Scientifique
SO PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2006037028 | A2 | 20060406 | WO 2005-US34786 | 20050926 |
| WO 2006037028 | A3 | 20060713 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2004-613085P P 20040924
OS MARPAT 144:331664
AB Nucleoside analogs I, wherein R1 is H, alkyl, acyl, phosphate A method and composition for treating a host infected with flavivirus, pestivirus or hepacivirus comprising administering an effective flavivirus, pestivirus or hepacivirus treatment amount of a described base-modified nucleoside or a pharmaceutically acceptable salt or prodrug thereof, is provided. Thus, nucleoside I (X = W = O, R1 = R2 = R4 = R6 = R7 = B = H; R3 = R5 = OH; Y = N; A = COOMe) was prepared as antiviral agents for treating flaviviruses, pestiviruses and hepacivirus and in particular for hepatitis C virus

infection. (no biol. data). Anti-flavivirus, pestivirus or hepacivirus activity, bioavailability in Cynomolgus monkeys, bone marrow toxicity, mitochondria toxicity, and cytotoxicity of title nucleosides were reported (no biol. data). These nucleosides can be assessed for their ability to inhibit flavivirus, pestivirus or hepacivirus polymerase activity in vitro according to standard screening methods.

L11 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2006:15810 CAPLUS
DN 144:108550
TI Preparation of 5-aza-7-deazadeazapurine and C-branched **nucleosides** as antiviral agents for treating **Flaviviridae**
IN **Gosselin, Gilles**; La Colla, Paolo; Seela, Frank; **Storer, Richard**; Dukhan, David; Leroy, Frederic
PA Idenix (Cayman) Limited, Cayman I.
SO PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2006000922 | A2 | 20060105 | WO 2005-IB2768 | 20050623 |
| WO 2006000922 | A3 | 20060526 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

| | | | | |
|---|---|---|---|---|
| US 2006040944 | A1 | 20060223 | US 2005-166498 | 20050623 |
| PRAI US 2004-582182P | P | 20040623 | | |

OS MARPAT 144:108550
AB This invention is directed to a method for treating a host, especially a human, infected with hepatitis C, flavivirus and/or pestivirus, comprising administering to that host an effective amount of an anti-flavivirus or anti-pestivirus, biol. active 5-aza-7-deazadeazapurine and C-branched nucleosides I-VI, wherein A, B, and Y, each independently is H, halogen,OR1, S(O)n, S(O)nR1, S(O)nR1R2, NR1R2, NR, CN, CF3, CR1R2, C(W)OR1, C(W)SR1, C(W)NR1R2, NO2, N3, cyclic or acyclic, branched or unbranched alkyl, alkenyl, alkynyl, aryl, aralkyl, heterocycle; or A and B taken together with the carbon atoms to which they are attached may form a 4-7 membered carbocyclic or heterocyclic ring; Z is O, S, NR1, or CR1R2; each V is independently N or CR1; each R1 and R2 independently is H; C cyclic or acyclic, branched or unbranched alkyl, alkenyl, alkynyl, halo, O-alkyl, NH2, NHMe, NMe2, CN, acyl, aryl, heteroaryl, heterocycle, carbocycle, amino acid residue, or together with the atoms to which they are attached may form a 3-7 membered carbocyclic or heterocyclic ring; each W is independently O, S, or NR1; R is independently H; sugar residue, cyclic or acyclic, branched or unbranched alkyl, alkenyl, alkynyl, acyl, aryl, or aralkyl; n is independently 0- 2; . The 5-aza-7-deazapurine moiety may be substituted or un-substituted, and may comprise a non-nucleoside or nucleoside analog, or a salt or prodrug thereof. The compound of the present invention may be administered alone or in

combination with another anti-hepatitis C, anti-flavivirus and/or anti-pestivirus agent. Thus, 2-amino-8-(β-D-2-deoxyribofuranosyl)-imidazo[1.2-a]-s-triazin-4-one was prepared and tested in Cynomolgus monkeys as antiviral agent for treating Flaviviridae (EC50 > 100 μM).

L11 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:1151367 CAPLUS
TI Synthesis of 5-aza-7-deazaguanine **nucleoside** derivatives as potential anti-**flavivirus** agents
AU Dukhan, D.; Leroy, F.; Peyronnet, J.; Bosc, E.; Chaves, D.; Durka, M.; **Storer, R.**; La Colla, P.; Seela, F.; **Gosselin, G.**
CS Laboratoire Cooperatif Idenix, CNRS, Universite Montpellier II, Montpellier, 5, Fr.
SO Nucleosides, Nucleotides & Nucleic Acids (2005), 24(5-7), 671-674
CODEN: NNNAFY; ISSN: 1525-7770
PB Taylor & Francis, Inc.
DT Journal
LA English
AB Coupling suitable sugars (D- or L-ribofuranose, 2'- or 3'-deoxy sugar, branched sugars) with 2-aminoimidazo[1,2-a]-s-triazin-4-one was carried out via condensation in the presence of sodium hydride or condensation using Vorbruggen's methods. The 5-aza-7-deazaguanine nucleoside analogs, e.g. I, obtained were evaluated in cell culture expts. for the inhibition of the replication of a number of RNA viruses, including BVDV, YFV, and WNV. Modest but selective activity against BVDV was found for the β-D-ribo- and 2'-deoxy-β-D-ribo- ribofuranosyl derivs., without cytotoxicity up to 100 μM.
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:99345 CAPLUS
DN 142:177053
TI Preparation of purine **nucleoside** analogs for treating **flaviviridae** including hepatitis C
IN **Storer, Richard**; **Gosselin, Gilles**; Dukhan, David; Leroy, Frederic
PA Idenix Cayman Limited, Cayman I.; Centre National De La Recherche Scientifique; L'universite Montpellier II
SO PCT Int. Appl., 139 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2005009418 | A2 | 20050203 | WO 2004-IB2703 | 20040726 |
| WO 2005009418 | A3 | 20050407 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|---|---|---|---|---|
| AU 2004258750 | A1 | 20050203 | AU 2004-258750 | 20040726 |

| | | | | | |
|---|---|---|---|---|---|
| | CA 2533367 | AA | 20050203 | CA 2004-2533367 | 20040726 |
| | US 2005075309 | A1 | 20050407 | US 2004-900008 | 20040726 |
| | EP 1658302 | A2 | 20060524 | EP 2004-744307 | 20040726 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR | | | | |
| | NO 2006000914 | A | 20060425 | NO 2006-914 | 20060224 |
| PRAI | US 2003-490216P | P | 20030725 | | |
| | WO 2004-IB2703 | W | 20040726 | | |

OS MARPAT 142:177053

AB Title nucleosides I, wherein B is nucleobase; R is H, mono-, di-, or tri-phosphate, a stabilized phosphate, or phosphonate; X is O, S[O]n, CH, CHOH, substituted CH , NH, N-alkyl, N-alkenyl, N-alkynyl, S(O)N-alkyl, S(O)N-alkenyl, S(O)N-alkynyl, SCH-halogen; n is 0-2; R1 and R1' are independently H, OH, alkyl, azido, cyano, alkenyl, alkynyl, C(O)O-(alkyl), C(O)O-(alkenyl), C(O)O-(alkynyl), O(acyl), O(alkyl), O(alkenyl), O(alkynyl), halogen, NO2, NH2, NH-alkyl, NH(acyl), amide, S(O)N-alkyl, S(O)N-alkenyl, S(O)N-alkynyl, SCH-halogen; X is O, S[O]n, NH, N-alkyl, N-alkenyl, N-alkynyl, S(O)N-alkyl, S(O)N-alkenyl, S(O)N-alkynyl, or SCH-halogen; R2 and R3 are independently OH, NH2, SH, halogen, CN, NO2, amide, N3, alkyl, alkenyl, alkynyl, C(O)O-(alkyl), C(O)O-(alkenyl), C(O)O-(alkynyl), O(acyl), O(alkyl), O(alkenyl), O(alkynyl), OC(O)NH, NC, C(O)OH, SCN, OCN, S(alkyl), S(alkenyl), S(alkynyl), NH(alkyl), NH(alkenyl), NH(alkynyl), an amino acid residue, a prodrug or leaving group that provides OH in vivo, or an 3-7 membered heterocyclic ring having O, S and/or N independently as a heteroatom taken alone or in combination; R2' and R3' are independently H; alkyl, alkenyl, or alkynyl; C(O)O(alkyl), C(O)O(alkenyl), C(O)O(alkynyl), amide, O(acyl), O(alkyl), O(alkenyl), halogen, halogenated alkyl and particularly CF3, azido, cyano, NO2, S(alkyl), S(alkenyl), S(alkynyl), NH2, NH(alkyl), NH(alkenyl), NH(alkynyl), NH(acyl) were prepared as antiviral agents. This invention is directed to a method for treating a host, especially a human, infected with hepatitis C, flavivirus and/or pestivirus, comprising administering to that host an effective amount of an anti-HCV biol. active pentofuranonucleoside where the pentofuranonucleoside base is an optionally substituted 2-azapurine. The optionally substituted pentofuranonucleoside, or a salt or prodrug thereof, may be administered alone or in combination with one or more optionally substituted pentofuranonucleosides or other anti-viral agents. Thus, purine nucleoside II.2HCl was prepared and tested in vitro as antiviral agent. The antiviral agent is selected from the group consisting of an interferon, ribavirin, an interleukin, an NS3 protease inhibitor, a cysteine protease inhibitor, phenanthrenequinone, a thiazolidine derivative, a thiazolidine and a benzanilide, a helicase inhibitor, a polymerase inhibitor, a nucleotide analog, gliotoxin, cerulenin, an antisense phosphorothioate oligodeoxyribonucleotide, an inhibitor of 1RES-dependent translation, and a ribozyme.

L11 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:965042 CAPLUS

DN 141:395766

TI Preparation of 5-aza-7-deazapurine **nucleosides** as antiviral agents for treating **flaviviridae**

IN La Colla, Paolo; **Gosselin, Gilles**; Seela, Frank; Dukhan, David; Leroy, Frederic

PA Universita Degli Studi di Cagliari, Italy; Centre National de la Recherche Scientifique; Universitat Osnabruck Laboratorium fur Organic and Biorganic Chemie

SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2

DT Patent

LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2004096197 | A2 | 20041111 | WO 2004-IB1740 | 20040503 |
| | WO 2004096197 | A3 | 20050113 | | |
| | WO 2004096197 | C1 | 20050414 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO

<------User Break------>

=> d bib ab l11 5-13

L11 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:965042 CAPLUS
DN 141:395766
TI Preparation of 5-aza-7-deazapurine **nucleosides** as antiviral agents for treating **flaviviridae**
IN La Colla, Paolo; **Gosselin, Gilles**; Seela, Frank; Dukhan, David; Leroy, Frederic
PA Universita Degli Studi di Cagliari, Italy; Centre National de la Recherche Scientifique; Universitat Osnabruck Laboratorium fur Organic and Biorganic Chemie
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2004096197 | A2 | 20041111 | WO 2004-IB1740 | 20040503 |
| | WO 2004096197 | A3 | 20050113 | | |
| | WO 2004096197 | C1 | 20050414 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2003-467465P P 20030502
OS MARPAT 141:395766
AB This invention is directed to a method for treating a host, especially a human, infected with hepatitis C, flavivirus and/or pestivirus, comprising administering to that host an effective amount of an anti-hepacivirus, anti-flavivirus or anti-pestivirus biol. active acyclic ester or pentofurano-nucleoside that has a 5-aza-7-deazapurine nucleoside base I, wherein R1 is OH, phosphate or phosphonate, acyl, H, alkyl, sulfonate ester including alkyl or arylalkyl-sulfonyl including methanesulfonyl and benzyl, wherein the Ph group is optionally substituted with one or more substituents as described in the definition of an aryl given herein; arylsulfonyl; lipid, phospholipid; amino acid; carbohydrate; peptide; cholesterol; any of which may be O-linked; or another pharmaceutically

acceptable leaving group that when administered in vivo, provides a compound wherein R1 is independently OH or O-phosphate; each R2 and R3 independently is H or OH; Z is H, OH, SH, NH2, halo, CF3, alkyl, alkylamino, cyclo-alkylamino, alkoxy; Y is O, S, or NR4; and R4 is independently hydrogen, alkyl, halo-alkyl, alkenyl, halo-alkenyl, aryl, arylalkyl, Ph or benzyl, acyl. Also claimed are pharmaceutical compns. of the present invention that may be administered alone or in combination and/or alternation with another antiviral agent, and a use of these nucleoside analogs in the manufacture of a medicament. Thus, 2-amino-8-(5-deoxy-3-D-ribofuranosyl)imidazo-[1,2-a]-s-triazin-4-one was prepared and tested in vitro as antiviral agent. Compds. can exhibit anti-flavivirus or pestivirus activity by inhibiting flavivirus or pestivirus polymerase.

L11 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:453348 CAPLUS
DN 141:17578
TI Treatment of **Flaviviridae** infection with 2'-branched **nucleosides** and another mutation-inducing drug such as interferon
IN **Sommadossi, Jean-Pierre**; La Colla, Paolo; Standring, David; Bichko, Vadim; Qu, Lin
PA Idenix (Cayman) Limited, Cayman I.; Universita Degli Studi Di Cagliari
SO PCT Int. Appl., 166 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2004046331 | A2 | 20040603 | WO 2003-US36714 | 20031117 |
| | WO 2004046331 | A3 | 20060302 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2506129 | AA | 20040603 | CA 2003-2506129 | 20031117 |
| | AU 2003298658 | A1 | 20040615 | AU 2003-298658 | 20031117 |
| | US 2005031588 | A1 | 20050210 | US 2003-715729 | 20031117 |
| | EP 1576138 | A2 | 20050921 | EP 2003-796412 | 20031117 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| | BR 2003016363 | A | 20051004 | BR 2003-16363 | 20031117 |
| | JP 2006519753 | T2 | 20060831 | JP 2004-553823 | 20031117 |
| | NO 2005002920 | A | 20050815 | NO 2005-2920 | 20050615 |
| PRAI | US 2002-426675P | P | 20021115 | | |
| | WO 2003-US36714 | W | 20031117 | | |

OS MARPAT 141:17578
AB The present invention discloses a method for the treatment of Flaviviridae infection that includes the administration of a 2'-branched nucleoside, or a pharmaceutically acceptable prodrug and/or salt thereof, to a human in need of therapy in combination or alternation with a drug that directly or indirectly induces a mutation in the viral genome at a location other than a mutation of a nucleotide that results in a change from serine to a different amino acid in the highly conserved consensus sequence,

XRX<u>S</u>GXXXT, of domain B of the RNA polymerase region, or is associated with such a mutation. The invention also includes a method to detect a mutant strain of Flaviviridae and a method for its treatment. Thus, in bovine viral diarrhea virus (BVDV)-infected MDBK cells treated with β-D-2'-methylcytidine, viruses resistant to the nucleoside appeared. The drug resistance was associated with a mutation in the NS5B gene which resulted in an S405T substitution in the encoded RNA-dependent RNA polymerase. These mutant viruses were sensitive to Intron A (interferon α-2b). Intron A and β-D-2'-methylcytidine exhibited synergistic inhibitory activity on BVDV growth in MDBK cells.

L11 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:20697 CAPLUS
DN 140:87662
TI 2'- and 3'-**nucleoside** prodrugs for treating **Flaviviridae** infections
IN **Sommadossi, Jean-pierre**; La Colla, Paolo; **Storer, Richard**; **Gosselin, Gilles**
PA Idenix (Cayman) Limited, Cayman I.; Centre National de la Recherche Scientifique; Universita Degli Studi di Cagliari
SO PCT Int. Appl., 2498 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2004003000 | A2 | 20040108 | WO 2003-IB3901 | 20030627 |
| | WO 2004003000 | A3 | 20041104 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2490200 | AA | 20040108 | CA 2003-2490200 | 20030627 |
| | AU 2003263412 | A1 | 20040119 | AU 2003-263412 | 20030627 |
| | EP 1525209 | A2 | 20050427 | EP 2003-761749 | 20030627 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| | CN 1678621 | A | 20051005 | CN 2003-820690 | 20030627 |
| | JP 2005537242 | T2 | 20051208 | JP 2004-517162 | 20030627 |
| | CN 1761677 | A | 20060419 | CN 2003-820501 | 20030627 |
| | WO 2005020884 | A2 | 20050310 | WO 2004-US15395 | 20040514 |
| | WO 2005020884 | A3 | 20060622 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |

| | | | | | |
|---|---|---|---|---|---|
| | EP 1656093 | A2 | 20060517 | EP 2004-776022 | 20040514 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR | | | | |
| | NO 2005000466 | A | 20050323 | NO 2005-466 | 20050127 |
| PRAI | US 2002-392350P | P | 20020628 | | |
| | US 2002-392351P | P | 20020628 | | |
| | US 2003-466194P | P | 20030428 | | |
| | US 2003-470949P | P | 20030514 | | |
| | WO 2003-IB3901 | W | 20030627 | | |
| | WO 2004-US15395 | W | 20040514 | | |

OS MARPAT 140:87662

AB 2' And 3'-Prodrugs of 1'-, 2'-, 3'-, or 4'-branched β-D or β-L nucleosides, or their pharmaceutically acceptable salts and derivs., are described which are useful in the prevention and treatment of Flaviviridae infections and other related conditions. These modified nucleosides provide superior results against flaviviruses and pestiviruses, including hepatitis C virus and viruses generally that replicate through an RNA-dependent RNA reverse transcriptase. Compds., compns., methods and uses are provided for the treatment of Flaviviridae infection, including HCV infection, that include the administration of an effective amount of the prodrugs of the invention, or their pharmaceutically acceptable salts or derivs. These drugs may optionally be administered in combination or alternation with further antiviral agents to prevent or treat Flaviviridae infections and other related conditions. Preparation of compds. of the invention is included.

L11 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:20696 CAPLUS

DN 140:77365

TI Preparation of modified 2'- and 3'-**nucleoside** prodrugs for treating **Flaviviridae** infections

IN **Sommadossi, Jean-pierre**; La Colla, Poalo; **Storer, Richard**; **Gosselin, Gilles**

PA Idenix (Cayman) Limited, Cayman I.; Universita degli studi di Cagliari; Centre National de la Recherche Scientifique

SO PCT Int. Appl., 201 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 4

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2004002999 | A2 | 20040108 | WO 2003-IB3246 | 20030627 |
| | WO 2004002999 | A3 | 20040812 | | |
| | WO 2004002999 | C1 | 20050217 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2490191 | AA | 20040108 | CA 2003-2490191 | 20030627 |
| | AU 2003247084 | A1 | 20040119 | AU 2003-247084 | 20030627 |
| | EP 1523489 | A2 | 20050420 | EP 2003-761744 | 20030627 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |

| | | | | | |
|---|---|---|---|---|---|
| CN 1678621 | A | 20051005 | CN 2003-820690 | 20030627 |
| JP 2005533817 | T2 | 20051110 | JP 2004-517158 | 20030627 |
| CN 1761677 | A | 20060419 | CN 2003-820501 | 20030627 |
| WO 2005020884 | A2 | 20050310 | WO 2004-US15395 | 20040514 |
| WO 2005020884 | A3 | 20060622 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|---|---|---|---|---|
| EP 1656093 | A2 | 20060517 | EP 2004-776022 | 20040514 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR

| | | | | |
|---|---|---|---|---|
| NO 2005000465 | A | 20050127 | NO 2005-465 | 20050127 |
| PRAI US 2002-392350P | P | 20020628 | | |
| US 2002-392351P | P | 20020628 | | |
| US 2003-466194P | P | 20030428 | | |
| US 2003-470949P | P | 20030514 | | |
| WO 2003-IB3246 | W | 20030627 | | |
| WO 2004-US15395 | W | 20040514 | | |

OS MARPAT 140:77365

AB 2' And/or 3' prodrugs of 1', 2', 3' or 4'-branched-nucleosides I, wherein R1-R3 are independently H, phosphate, alkyl, acyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, CO-aryloxyalkyl, CO-substituted aryl, sulfonate ester, benzyl, wherein the Ph group is optionally substituted with one or more substituents, alkylsulfonyl, arylsulfonyl, aralkylsulfonyl, lipid, amino acid, carbohydrate, peptide, cholesterol; Y1 is hydrogen, bromo, chloro, fluoro, iodo, CN, OH, OR4, NH2, NHR4, NR4R5, SH or SR4; X1 and X2 are independently alkyl, CH3, CF3, CY3, 2-Br-Et, CH2F, CH2Cl, CH2CF3, CF2CF3, CY2CY3, CH2OH, alkenyl, alkynyl, COOH, COOR4, COO-alkyl, COO-aryl, CO-O-alkoxyalkyl, CONH2, CONHR4, CON(R4)2, halo, CN, N3, OH, OR4, NH2, NHR4, NR4R5, SH or SR5; Y is independently H, halo; and each R4 and R5 is independently hydrogen, acyl, alkyl, lower alkyl, alkenyl, alkynyl or cycloalkyl, and their pharmaceutically acceptable salts and derivs. are described. These prodrugs are useful in the prevention and treatment of Flaviviridae infections, including HCV infection, and other related conditions. Compds. and compns. of the prodrugs of the present invention are described. Methods and uses are also provided that include the administration of an effective amount of the prodrugs of the present invention, or their pharmaceutically acceptable salts or derivs. These drugs may optionally be administered in combination or alteration with further anti-viral agents to prevent or treat Flaviviridae infections and other related conditions. Thus, antiviral activity of β-D-2'-C-methyl-7-methyl-6-phenyl-3,3a,5,8a-tetrahydro-1,3,4,5,7a-penta-aza-s-indacen-8-one is reported.

L11 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:20443 CAPLUS

DN 140:70984

TI 2'-C-methyl-3'-O-L-valine ester ribofuranosyl cytidine for treatment of **flaviviridae** infections

IN **Sommadossi, Jean-Pierre**; La Colla, Paolo

PA Idenix (Cayman) Limited, Cayman I.; Universita Degli Studi di Cagliari

SO PCT Int. Appl., 110 pp.

CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2004002422 | A2 | 20040108 | WO 2003-US20431 | 20030627 |
| | WO 2004002422 | A3 | 20050407 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2489552 | AA | 20040108 | CA 2003-2489552 | 20030627 |
| | AU 2003248748 | A1 | 20040119 | AU 2003-248748 | 20030627 |
| | US 2004077587 | A1 | 20040422 | US 2003-607909 | 20030627 |
| | EP 1536804 | A2 | 20050608 | EP 2003-762183 | 20030627 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| | CN 1678326 | A | 20051005 | CN 2003-820701 | 20030627 |
| | JP 2005533824 | T2 | 20051110 | JP 2004-518041 | 20030627 |
| | WO 2005020884 | A2 | 20050310 | WO 2004-US15395 | 20040514 |
| | WO 2005020884 | A3 | 20060622 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | EP 1656093 | A2 | 20060517 | EP 2004-776022 | 20040514 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR | | | | |
| | NO 2005000490 | A | 20050127 | NO 2005-490 | 20050127 |
| PRAI | US 2002-392351P | P | 20020628 | | |
| | US 2003-466194P | P | 20030428 | | |
| | US 2003-470949P | P | 20030514 | | |
| | WO 2003-US20431 | W | 20030627 | | |
| | WO 2004-US15395 | W | 20040514 | | |

OS MARPAT 140:70984

AB The 3'-L-valine ester of β-D-2'-C-methyl-ribofuranosyl cytidine provides superior results against flaviviruses and pestiviruses, including hepatitis C virus. Based on this discovery, compds., compns., methods and uses are provided for the treatment of flaviviridae, including HCV, that include the administration of an effective amount of val-mCyd or its salt, ester, prodrug or derivative, optionally in a pharmaceutically acceptable carrier. In an alternative embodiment, val-mCyd is used to treat any virus that replicates through an RNA-dependent RNA polymerase. Several examples are provided of the pharmacol., mechanism of action, metabolism, side effects, and clin. efficacy of the title compound

L11 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:261692 CAPLUS
DN 138:265611
TI Methods and compositions for treating **flaviviruses** and pestiviruses using 4'-modified **nucleosides**, and preparation thereof
IN **Gosselin, Gilles**; Imbach, Jean-Louis; **Sommadossi, Jean-Pierre**
PA Idenix (Cayman) Limited, Cayman I.; Centre National de la Recherche Scientifique; L'Universite Montpellier II
SO PCT Int. Appl., 159 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2003026675 | A1 | 20030403 | WO 2002-US31203 | 20020930 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2004006002 | A1 | 20040108 | US 2002-261327 | 20020930 |
| EP 1438054 | A1 | 20040721 | EP 2002-770551 | 20020930 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| JP 2005536440 | T2 | 20051202 | JP 2003-530310 | 20020930 |
| PRAI US 2001-326192P | P | 20010928 | | |
| WO 2002-US31203 | W | 20020930 | | |

OS MARPAT 138:265611
AB A method and composition are provided for treating a host infected with flavivirus or pestivirus, comprising administering an effective amount of a 4'-modified nucleoside, or a pharmaceutically acceptable salt or prodrug thereof. Preparation of nucleoside derivs. is described.
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:886155 CAPLUS
DN 136:590
TI Methods and compositions using modified **nucleosides** for treating **flaviviruses** and pestiviruses
IN **Sommadossi, Jean-Pierre**; Lacolla, Paolo
PA Novirio Pharmaceuticals Limited, Cayman I.; Universita Degli Studi Di Cagliari
SO PCT Int. Appl., 302 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2001092282 | A2 | 20011206 | WO 2001-US16687 | 20010523 |
| WO 2001092282 | A3 | 20020502 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | | | |
|---|---|---|---|---|---|
| CA 2410579 | AA | 20011206 | CA 2001-2410579 | 20010523 |
| EP 1294735 | A2 | 20030326 | EP 2001-952131 | 20010523 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| US 2003060400 | A1 | 20030327 | US 2001-863816 | 20010523 |
| US 6812219 | B2 | 20041102 | | |
| BR 2001011196 | A | 20040406 | BR 2001-11196 | 20010523 |
| JP 2004510698 | T2 | 20040408 | JP 2002-500895 | 20010523 |
| NO 2002005600 | A | 20030117 | NO 2002-5600 | 20021121 |
| ZA 2002010112 | A | 20040623 | ZA 2002-10112 | 20021212 |
| US 2004063622 | A1 | 20040401 | US 2003-602693 | 20030620 |
| US 2004097462 | A1 | 20040520 | US 2003-602692 | 20030620 |
| US 7101861 | B2 | 20060905 | | |
| US 2004102414 | A1 | 20040527 | US 2003-602694 | 20030620 |
| US 2006166865 | A1 | 20060727 | US 2003-602135 | 20030620 |
| PRAI US 2000-207674P | P | 20000526 | | |
| US 2001-283276P | P | 20010411 | | |
| US 2001-863816 | A3 | 20010523 | | |
| WO 2001-US16687 | W | 20010523 | | |

OS MARPAT 136:590

AB A method and composition are provided for treating a host infected with flavivirus or pestivirus, comprising administering an effective amount of a 1', 2' or 3'-modified nucleoside or a pharmaceutically acceptable salt or prodrug thereof.

L11 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:617773 CAPLUS
DN 135:175346
TI Method for the treatment or prevention of **flavivirus** infections using **nucleoside** analogues
IN Ismaili, Hicham Moulay Alaoui; Cheng, Yun-Xing; Lavallee, Jean-Francois; Siddiqui, Arshad; **Storer, Richard**
PA Biochem Pharma Inc., Can.
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2001060315 | A2 | 20010823 | WO 2001-CA197 | 20010219 |
| WO 2001060315 | A3 | 20030116 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | | | |
|---|---|---|---|---|---|
| | CA 2400274 | AA | 20010823 | CA 2001-2400274 | 20010219 |
| | AU 2001035278 | A5 | 20010827 | AU 2001-35278 | 20010219 |
| | EP 1296690 | A2 | 20030402 | EP 2001-907276 | 20010219 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| | JP 2003523978 | T2 | 20030812 | JP 2001-559414 | 20010219 |
| | NZ 521210 | A | 20041126 | NZ 2001-521210 | 20010219 |
| | US 2002019363 | A1 | 20020214 | US 2001-785235 | 20010220 |
| | US 6784161 | B2 | 20040831 | | |
| | ZA 2002006506 | A | 20031114 | ZA 2002-6506 | 20020814 |
| | NO 2002003884 | A | 20021017 | NO 2002-3884 | 20020816 |
| | US 2004248844 | A1 | 20041209 | US 2004-887292 | 20040709 |
| PRAI | US 2000-183349P | P | 20000218 | | |
| | WO 2001-CA197 | W | 20010219 | | |
| | US 2001-785235 | A1 | 20010220 | | |

OS MARPAT 135:175346

AB The present invention relates to a method for the treatment or prevention of Flavivirus infections using nucleoside analogs in a host comprising administering a therapeutically effective amount of the nucleoside analog or a pharmaceutically acceptable salt thereof.

L11 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2001:338330 CAPLUS

DN 134:348243

TI Method for the treatment or prevention of **Flaviviridae** viral infection using **nucleoside** analogs

IN **Storer, Richard**

PA Biochem Pharma Inc., Can.

SO PCT Int. Appl., 76 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2001032153 | A2 | 20010510 | WO 2000-CA1316 | 20001103 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2389745 | AA | 20010510 | CA 2000-2389745 | 20001103 |
| | EP 1225899 | A2 | 20020731 | EP 2000-974218 | 20001103 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| | US 6566365 | B1 | 20030520 | US 2000-704832 | 20001103 |
| | US 2003225037 | A1 | 20031204 | US 2003-397167 | 20030327 |
| PRAI | US 1999-163394P | P | 19991104 | | |
| | US 1999-163405P | P | 19991104 | | |
| | US 2000-704832 | A3 | 20001103 | | |
| | WO 2000-CA1316 | W | 20001103 | | |

OS MARPAT 134:348243

AB A method is provided for treating or preventing a Flaviviridae viral infection in a host comprising administering a therapeutically effective amount of at least one nucleoside analog (Markush included). Preparation of nucleoside analogs is described.

```
=> d his ful

     (FILE 'REGISTRY' ENTERED AT 09:28:39 ON 07 SEP 2006)
                DEL HIS Y
                ACT MCINTOSH/A
               ---------
L1              STR
L2            25 SEA SSS FUL L1
                ---------

     FILE 'CAPLUS' ENTERED AT 09:29:29 ON 07 SEP 2006
L3             7 SEA ABB=ON  PLU=ON  L2
                D SCAN TI

     FILE 'REGISTRY' ENTERED AT 09:30:46 ON 07 SEP 2006
                D QUE STAT L2
                D QUE STAT L2

     FILE 'REGISTRY' ENTERED AT 09:32:47 ON 07 SEP 2006
                D QUE STAT L2

     FILE 'CAPLUS' ENTERED AT 09:32:53 ON 07 SEP 2006
                D QUE NOS L3
                D .CA HITSTR L3 1-7
                E STORER R/AU
L4           229 SEA ABB=ON  PLU=ON  STORER R?/AU
                E GOSSELIN G?/AU
L5           317 SEA ABB=ON  PLU=ON  GOSSELIN G?/AU
L6           213 SEA ABB=ON  PLU=ON  SOMMADOSSI J?/AU
L7           694 SEA ABB=ON  PLU=ON  (L4 OR L5 OR L6)
L*** DEL       0 S L7 AND L2
L8             0 SEA ABB=ON  PLU=ON  L7 AND L3
L9        411390 SEA ABB=ON  PLU=ON  NUCLEOTID?/OBI OR NUCLEOSID?/OBI OR
                FLAVIVIR?/OBI
L10          242 SEA ABB=ON  PLU=ON  L9 AND L7
L*** DEL       0 S L10 AND FLAVIR?
L11           13 SEA ABB=ON  PLU=ON  L10 AND FLAVIVIR?/OBI
                D QUE STAT NOS L11
                D BIB AB L11 1-13
                D BIB AB L11 5-13


     FILE CAPLUS

     Copyright of the articles to which records in this database refer is
     held by the publishers listed in the PUBLISHER (PB) field (available
     for records published or updated in Chemical Abstracts after December
     26, 1996), unless otherwise indicated in the original publications.
     The CA Lexicon is the copyrighted intellectual property of the
     American Chemical Society and is provided to assist you in searching
     databases on STN.  Any dissemination, distribution, copying, or storing
     of this information, without the prior written consent of CAS, is
     strictly prohibited.

     FILE COVERS 1907 - 7 Sep 2006  VOL 145 ISS 11
     FILE LAST UPDATED: 6 Sep 2006  (20060906/ED)

     Effective October 17, 2005, revised CAS Information Use Policies apply.
     They are available for your review at:
```

http://www.cas.org/infopolicy.html

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 6 SEP 2006 HIGHEST RN 905963-91-9
DICTIONARY FILE UPDATES: 6 SEP 2006 HIGHEST RN 905963-91-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>